REMARKS

I. Status of the Application and Claims

Applicant respectfully requests reconsideration and further examination in view of the following remarks.

Claims 133-139, 141-148, and 152-158 are pending in this application. Claims 140 and 149-151, directed to non-elected subject matter, have been canceled without prejudice or disclaimer. Applicant reserves the right to pursue the subject matter of the canceled claims in one or more divisional applications. Claims 133 and 141 are amended to delete the reference to at least one mutation in the pir gene leucine zipper-like motif and to recite that the "heterologous *pir* gene having at least one mutation in the *pir* gene DNA binding region encodes a π protein that activates the conditional origin of replication." Support for this amendment can be found throughout the specification, including, for example, at page 6, lines 10-18; page 16, line 25 to page 17, line 5; pages 65-68 (Example 13); and in the original claims, including claim 1.

Claim 142 is amended to recite that the heterologous *pir* gene "further" comprises at least one mutation in the leucine-zipper motif. Claim 143 is amended to recite that the heterologous *pir* gene further comprises a mutation in the "copy number control" region. Support for these amendments is found throughout the specification, including, for example, at page 16, line 25 to page 17, line 16.

Claims 152-158 have been added. Support for claims 152-158 is found throughout the specification, including, for example, at pages 17 and 65-68 (Example 13). These amendments do not introduce new matter into the claims.

II. Priority

The Office notes that "although the oath/declaration claims priority to [prior applications 10/268,948; 09/043,193, PCT/FR96/01414, and FR95/10825], Applicant has requested the cancellation of the first lines of the specification which contain a statement of these applications in a paper filed 1/27/06." Office action at 4. As indicated in the Preliminary Amendment dated January 27, 2006, Applicant no longer seeks the benefit of the filing dates of the earlier-filed applications. Accordingly, the reference to those applications was deleted from the first paragraph of the specification. Therefore, the effective filing date of this application is October 15, 2003.

III. Claim Objections

The Office objected to claims 135 and 143 under 37 C.F.R. § 1.75(c) as being of improper dependent form for allegedly failing to further limit the subject matter of a previous claim. Office action at 4-5. Claim 135 depends from claim 133 and claim 143 depends from claim 141. As amended, claims 133 and 141 recite that the heterologous *pir* gene has at least one mutation in the *pir* gene DNA binding region. Claim 135 now recites that the plasmid further comprises a mutation in the *pir* gene "copy number control region." Similarly, claim 143 now recites that the heterologous *pir* gene further comprises a mutation in the *pir* gene "copy number control" region. As such, claims 135 and 143 properly depend from claims 133 and 141, respectively, and Applicant requests the Office to withdraw this objection.

IV. Rejections Under 35 U.S.C. § 112, First Paragraph

A. The Specification Enables the Pending Claims

The Office rejects claims 133-136 and 141-145 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Office action at 6-8. Applicant respectfully traverses this rejection.

The Office acknowledges that the specification is "enabling for particularly claimed mutations in the DNA binding domain of the pir gene . . ." but asserts that the specification "does not reasonably provide enablement for all mutations in the pir gene leucine zipper-like motif or the pir gene DNA binding region." *Id.* at 6. Noting that "[t]here is no functional limitation in the claims," the Office asserts that "[t]he claim encompasses an unreasonable number of inoperative genes, which the skilled artisan would not know how to use." *Id.* The Office further asserts:

> The only function disclosed or known for the pir gene is as encoding the Pi protein needed for replication of the R6K replicon. The skilled artisan would not know how to use non-identical genes on the basis of teachings in the prior art or specification unless they possessed the replication control function disclosed in the instant specification. The specification does not provide guidance for using mutants of the pir gene which do not have the disclosed function in replication. The claims are broad because they do not require the claimed plasmids and cells comprising the heterologous pir gene mutants to be identical to the disclosed mutations and because the claims have no functional limitation for the pir gene.

Id. at 7-8.

As noted above, the claims have been amended to recite that the heterologous *pir* gene having at least one mutation in the *pir* gene DNA binding region encodes a Pi protein that activates a conditional origin of replication. Thus, Applicant is not claiming *all* mutations in the *pir* gene DNA binding region. Rather, Applicant is claiming those mutations in the *pir* gene DNA binding region that encode a Pi protein that activates a conditional origin of replication. The specification enables the full scope of the pending claims.

To the extent the Office takes the position that the specification only enables those species that have been disclosed, it is well settled, even in the unpredictable arts, that section 112, first paragraph, does not require disclosure of every species encompassed by the claims. *See In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). As observed by the court in *Angstadt*:

> To require such a complete disclosure would apparently necessitate a patent application or applications with “thousands” of examples[.] More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed.

Id.

Accordingly, the relevant inquiry for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the specification, coupled with information known in the art, without undue experimentation. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). The test for undue experimentation does not depend on the amount of experimentation, since a considerable amount is permissible as long as it is routine. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988); *see also*, M.P.E.P. § 2164.06.

The claims recite mutant pir genes having at least one mutation within a specific and well-defined region of the gene, the DNA binding region. As acknowledged by the

Office, Applicant teaches at least three mutations in the DNA binding region of pir gene (114C, 100B, and 201C), each of which results in a functional pir gene and Pi protein. *Id.* at 7. It remains uncontroverted that the specification fully enables one of skill in the art to make the 114C, 100B, and 201C mutations. The question then becomes whether given Applicant's teaching of the previously unknown importance of these mutations in the DNA binding region of the *pir* gene, it would take undue experimentation merely to test other mutants for their biological activity. Applicant submits that such testing is not undue.

Applicant's disclosure provides considerable direction and guidance on how to practice the invention. In the present application, Applicant identifies at least three mutant *pir* genes having a mutation in the *pir* gene DNA binding region. In addition, Applicant describes how to generate mutant *pir* genes using known mutagenesis techniques. Specification, pp. 65-68. Next, Applicant explains how to use a simple screening assay to determine if the mutant *pir* genes encode Pi proteins that can activate a conditional origin of replication. *Id.* As explained in the specification, biological activity can be measured using a fluorescence-based screening assay, where the intensity of the fluorescence increases with plasmid copy number. *Id.* Applicant also provides working examples (Example 13), and identifies the mutants discussed above that were capable of activating a conditional origin of replication, including the 114C, 100B, and 201C mutations. *Id.*

Therefore, given Applicant's teaching in the specification, it would not require undue experimentation 1) to generate additional *pir* genes having at least one mutation in the DNA binding region and 2) to screen those mutated *pir* genes using the routine methods described in the specification to identify those encoding a π protein that activates a conditional origin of replication, as recited in the claims.

For these reasons, Applicant respectfully submits that the specification provides an enabling disclosure that is commensurate in scope with the claimed subject matter. Accordingly, Applicant requests withdrawal of this 35 U.S.C. § 112, first paragraph, rejection.

B. The Specification Provides Written Description Support for the Pending Claims

The Office rejects claims 133-136 and 141-145 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Office action at 5-6. Applicant respectfully traverses this rejection.

The Office asserts that "claims 133-136 and 141-145 are genus claims in terms of plasmids and cells comprising heterologous pir gene which contains mutations in the DNA binding domain and/or the leucine zipper-like motif, and does not limit the mutant genes to those which retain function in replication control." *Id.* Claims 133 and 141 have been amended to delete the reference to at least one mutation in the leucine zipper motif. Claims 133 and 141 have also been amended to clarify that the mutant *pir* gene retains a function. Specifically, Applicant amends claims 133 and 141 to recite that the heterologous *pir* gene having at least one mutation in the *pir* gene DNA binding domain encodes a π protein that activates a conditional origin of replication.

The written description requirement for a claimed genus may be satisfied by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show Applicant was in possession of the claimed invention. *See* M.P.E.P. § 2163, p. 2100-164; *see also*, *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002). This is precisely what Applicant has done here. Applicant adequately describes the claimed invention by combining both structural and functional characteristics.

Structurally, the *π* protein encoded by the *pir* gene is a well-characterized protein with defined regions, including the leucine-zipper motif, the copy number control region, and the DNA binding region, as set forth in Figure 11 of the specification. Independent claims 133 and 141 recite that the heterologous *pir* gene has at least one mutation in one of those three defined regions: the DNA binding region. Functionally, claims 133 and 141 recite that the encoded Pi protein activates a conditional origin of replication. Thus, claims 133 and 141 encompass a claimed genus of structurally-related mutant *pir* genes that encode Pi proteins possessing a specific function.

As acknowledged by the Office, Applicant teaches at least three different mutations in the DNA binding region of the pir gene that result in a functional pir gene and Pi protein, the 114C mutation, the 100B mutation, and the 201C mutation. *Id.* at 7. Thus, the specification demonstrates a correlation between function and structure sufficient to show Applicant was in possession of the claimed invention. Accordingly, Applicant requests that the Office withdraw this rejection.

V. Double Patenting Rejection

The Office provisionally rejects claims 141, 142, and 145 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 11-13, 21-23, 26, and 32-34 of copending Application 10/268,948. Office Action at 9. Applicant respectfully traverses this rejection.

According to the Office, copending Application 10/268,948 contains claims directed to recombinant cells comprising a heterologous replication initiation protein which is encoded by *pir* 116 *pir* 42. *Id.* The Office further notes that the *pir* 42 mutation is in the leucine zipper domain of *pir*. *Id.* As a result, the Office asserts that "the subject matter of the conflicting claims are encompassed by the claims of the instant application, which recites a *pir* gene having a mutation in the leucine zipper motif." *Id.*

Applicant has amended claims 133 and 141 by removing the reference to the at least one mutation in the "pir gene leucine zipper-like motif," rendering this rejection moot. Accordingly, Applicant respectfully requests that the Office withdraw this provisional double patenting rejection.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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